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Prevalence of GB Virus-C/Hepatitis G Virus Infection in an Antenatal Population

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It is difficult to explain the high levels of infection seen with GBV-C/HGV if transmission relies on the parenteral route. A group of young women was investigated in order to establish the prevalence of infection in this age group of the general population and perhaps indicate other possible routes of infection, searching for both GBV-C/HGV RNA and HGV E2 antibodies. Evidence of infection was found in 11.8%. This is a higher prevalence than that found in blood donors but lower than in prostitutes. Evidence is accumulating from various groups that sexual/close contact may result in transmission of this virus. ***J. Med. Virol. 57:235–237, 1999.***

KEY WORDS: GBV-C/HGV RNA; HGV anti-E2; prevalence of GBV-C/HGV; pooling sera; close contact

INTRODUCTION

GBV-C/HGV was described independently by two groups of workers in recent years [Simons et al., 1995; Linnen et al., 1996]. It is an RNA virus belonging to the *Flaviviridae* and is distantly related to hepatitis C. However, the clinical significance of infection with GBV-C/HGV is unclear. We have previously reported a high prevalence of GBV-C/HGV RNA in a multitransfused group of patients [Skidmore et al., 1997]; this and data from other studies [Jarvis et al., 1996] indicate that the overall prevalence of GBV-C/HGV within the population is likely to be higher than that of other recognized bloodborne infections. If these figures are confirmed, it would suggest that routes of transmission other than by blood, e.g., horizontal and vertical, may be important in maintaining this level of infection in the community.

The public health implications of GBV-C/HGV are consequent of an understanding of the natural history of the infection, together with a full assessment of its prevalence. Such data would be useful for predicting the significance of infection and be a basis for further studies. Figures for the overall prevalence of GBV-C/HGV have been based on small numbers of patients so that the confidence interval around the estimate is extremely wide. Initially, the virus could only be detected by reverse transcriptase–polymerase chain reaction (RT-PCR) but more recently an immunoassay for antibodies to a GBV-C/HGV envelope protein has been developed [Tacke et al., 1996]. We tested a group of antenatal patients to see how the prevalence of markers of GBV-C/HGV infection compares with other groups and the feasibility of pooling sera for testing was also assessed.

MATERIALS AND METHODS

Patients

Residual serum samples were collected from 600 antenatal patients attending clinics in Telford/Shrewsbury. Only information about the date of birth was documented, otherwise the samples were anonymized. It was deduced that a sample size of 600 would be sufficient to give accurate data, allowing a narrow 95% confidence interval to be obtained (e.g., 3% ± 1.4%). The average age of the patients was 28 years (range 14.7–41.5). Ethical approval for the study was obtained.

GBV-C/HGV-RNA Detection

GBV-C/HGV was detected in sera by RT-PCR. Pools of serum from five patients (100 μl from each) were prepared and RNA extracted from 100 μl of the serum pool with purescript (Gentra Systems, Minneapolis, MN). Complementary DNA was synthesized from 10 μl of RNA using random hexamers (Pharmacia Biotech, Piscataway, NJ) and Moloney murine leukemia virus reverse transcriptase (Promega, Madison, WI) PCR was performed using nested primers derived from the 5′UTR [Jarvis et al., 1996]. The PCR products were analyzed on a 2% agarose gel. Constituent samples of any pool containing GBV-C/HGV-RNA were tested individually as described above.

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Anti-HGenv Detection

The anti-HGenv enzyme immunoassay (Boehringer Mannheim, Mannheim, Germany) was carried out according to the manufacturer's instructions. This assay is based on the recombinant GBV-C/HGV envelope protein E2. Reactive samples, i.e., showing OD values above the cutoff value, were further tested using the confirmation test procedure. Single sera were tested since pooling resulted in very low positive OD values, which were difficult to interpret.

RESULTS

Thirty-nine out of 600 (6.5%; age range 18–41.5 years) were found positive for GBV-C/HGV-RNA; 32/600 (5.3%; age range 16–39 years) were confirmed reactive for anti-HGV E2. There were no samples that were positive for both markers. Overall, the exposure to GBV-C/HGV was 11.8%.

DISCUSSION

It has been shown that there is a high prevalence of GBV-C/HGV in patients receiving blood and blood products, therefore implicating the parenteral route in transmission of the virus. It has also been reported that GBV-C/HGV RNA is found in 3.2% of U.K. blood donors and that the total exposure of U.S. volunteer blood donors to GBV-C/HGV is 5.5% [Jarvis et al., 1996; Gutierrez et al., 1997]. Such reports suggest that GBV-C/HGV is present at a much higher level than other bloodborne infections. It is difficult to see how these high levels of infection are maintained by parenteral exposure alone and other routes of transmission must be important. Blood donors, however, are not representative of the general population since they are now very highly selected by medical history and self-deferral. We investigated a group of antenatal patients for both GBV-C/HGV RNA and anti-HGV E2 to try to determine the overall prevalence of infection in this age range of the general population.

Since RT-PCR assays are expensive and labor-intensive, it was decided to evaluate the usefulness of pooling samples prior to testing; this approach had previously been used by Corcoran et al. [1994]. Experience in our laboratory showed that viremic samples may be diluted at least 10-fold before GBV-C/HGV-RNA becomes undetectable by RT-PCR. Pools containing five sera were therefore employed. One hundred twenty pools were tested, of which 31 were reactive. The individual sera from each of these pools were then tested so that in total 275 tests were carried out. This was considerably fewer than the 600 individual sera that were included in the study and for epidemiological studies; pooling of sera, once evaluated has many advantages.

Clearly, this group represents a young, sexually active population and the results obtained (6.5% GBV-C/HGV RNA-positive plus 5.3% anti-HGV E2-reactive) suggest that sexual/close contact may play a role in transmission since this prevalence is higher than that seen in blood donors. A recent study [Kao et al., 1997] reports that spouses of GBV-C/HGV–infected patients are indeed at increased risk of acquiring the virus and Scallan et al. [1998] found a high prevalence of markers of GBV-C/HGV infection in prostitutes and male homosexuals, which provides strong evidence for the spread of GBV-C/HGV by sexual contact. The actual mechanism of this route of transmission still needs to be established, although Seemayer et al. [1998] have demonstrated a high prevalence of GBV-C/HGV RNA in saliva, which may contribute to the spread of infection, particularly where there is close contact.

Vertical transmission may also be significant. Early studies on small numbers of patients showed conflicting results [Feucht et al., 1996; Lin et al., 1996]. However, recent data from Hino et al. [1998] show a significantly higher level of mother-to-infant transmission of GBV-C/HGV than hepatitis C (HGV), although the exact route of transmission was not defined. None of the babies who were GBV-C/HGV RNA-positive had evidence of hepatitis. Since our study was carried out on an anonymized basis, this issue could not be addressed. Indeed, it was decided that since the clinical significance of infection with GBV-C/HGV is unclear, carrying out a survey that involved testing babies could not be justified.

The E2 region of GBV-C/HGV appears to be the only immunoreactive region of GBV-C/HGV that elicits an antibody response. Since GBV-C/HGV RNA and anti-HGV E2 are, in general, mutually exclusive, this suggests that antibody to GBV-C/HGV becomes detectable at the time of clearance of the virus and can be used as a marker of past infection. Whether it confers protection against infection remains to be determined. Both assays should therefore be carried out in order to assess the true exposure of a population to GBV-C/HGV. Persistence of GBV-C/HGV RNA and anti-HGV E2 have both been described. However, the determination of the duration of viral persistence and antibody response are essential to understanding the epidemiology of infection with GBV-C/HGV. Further prevalence studies using both markers in various groups should provide a picture of the major routes of transmission and give some insight into the clinical significance of infection with GBV-C/HGV.

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